egies. Implementing interventions to ameliorate cognitive impairments early in life may be a means for psychiatric prevention with substantial societal benefits beyond prevention of psychiatric outcomes (e.g., increasing the cognitive reserve in midlife may be a strategy to reduce dementia).

So, there are multiple challenges to implementing preventive strategies in psychiatry. There is, however, a clear need, and the time is ripe to make the leap towards primary and secondary prevention pathways in the critical period of early life and via cognition.

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Prevention in the mental health field should be implemented synergically at different levels

Fusar-Poli et al[1] present a comprehensive preventive framework for improving mental health in young people. Prevention in psychiatry is not a high funding priority, which is also reflected in the relatively low number of publications in the field. The responsibility for primary prevention and mental health promotion is placed in the social and educational sectors and, most often, the evidence base for initiatives is lacking.

In spite of research showing that risk of mental illness is associated with adversities during pregnancy and birth, low socioeconomic status, poor parenting skills, lack of stimulation and support during childhood, bullying, trauma, and early exposure to alcohol and drugs, initiatives to reduce these risk factors have attracted little scientific attention. Much can be done to improve the evidence base for early and broad preventive efforts.

Prevention of psychiatric disorders requires a coherent and multifaceted strategy, including at least five levels. The first is universal primary prevention to improve well-being (e.g., initiatives at the population level focusing on a healthy childhood, such as efforts to improve mental health literacy and parenting in early childhood). The second is universal primary prevention to prevent development of mental illness (e.g., interventions such as prevention of preterm birth and perinatal depression as well as initiatives to prevent bullying and traumatic childhood experiences and to reduce risk of adolescents engaging in substance abuse). The third is selective primary prevention to reduce risk of mental illness in risk groups (e.g., children born to parents with mental illness). The fourth is indicated primary prevention for young people showing signs or symptoms foreshadowing emerging disorder (e.g., clinical high-risk groups for psychosis or children with common mental health problems). The fifth is secondary prevention in early stages of psychiatric disorders (e.g., early intervention services in psychosis or early treatment of attention-deficit/hyperactivity disorder and autism spectrum disorders in child and adolescent services).

Here we focus briefly on selective interventions for families with parental mental illness and on indicated primary prevention initiatives, on the basis of the experience in Denmark.

Children born to parents with mental illnesses constitute an important risk group with a large prevention potential. Danish register-based figures indicate that every sixth child has a parent who has been diagnosed and treated in the secondary mental health sector. The true number at risk is likely to be even higher, since this does not include treatment in primary health care, nor those who, due to lack of accessible treatment offers, fail to be helped by health services. So, this is a very large number of children, who have been shown repeatedly to have a markedly increased risk of being diagnosed with a mental disorder before age 18[2,3], are more likely to live with a single parent[4], are at higher risk of having poor school performance[5], and have more neurocognitive, social and motor problems[6,7] than controls. Due to the parental mental illness, they are also more likely to experience insufficient support and stimulation in the home environment and to be exposed to traumatic life events – all factors that hamper their healthy developmental course.

Parental mental illness is often silenced in the family, passing on stigmatization across generations. Programmes directed towards the whole family should be developed and tested in order to change this trajectory that has been known for decades. Parental training and support as part of the recovery approach, collaboration of adult and child psychiatry with the primary sector, systematic family-based psychoeducation, and social, financial and practical support may be some elements potentially improving the functioning of the entire family and building resilience in the children at risk.

Concerning indicated prevention, implementation of transdiagnostic interventions are suggested to meet the needs of youths with common and multiple mental health problems. A Danish effectiveness study[8] documented the superiority of a new scalable transdiagnostic cognitive behavioral therapy (CBT), called "Mind My Mind" (MMM), compared to management as usual (MAU), for youths aged 6-16 years with emotional and/or behav-

ioral problems below the threshold for referral to mental health care.

A stage-based screening and stratification approach[9] was set up in non-specialized school-based services, with the dual goal to identify: a) the target group of youths with common emotional and/or behavioral problems; and b) those with emerging/severe mental illnesses, e.g. psychosis, who were supported to seek specialized care. The common treatment elements were "distilled" from evidence-based single-disorder CBT programs and organized into modules, materials, video-based feedback, supervision and training of the therapists to help them tailor the treatment to the individual subject.

The flexible and modular transdiagnostic implementation of CBT outperformed MAU on multiple endpoints, including reduced impact of mental health problems on functioning in daily life at the end of treatment, corresponding to a Cohen's effect size of 0.60. Harms were low and non-differential by the end of treatment, but significantly lower with MMM versus MAU at follow-up[8].

All the above-mentioned levels of prevention should be integrated in a common strategy. Interventions at different levels should be regarded not as contradictory, but as synergistic. Therefore, it is sad to witness psychiatrists spending time discussing, for example, the discontinuation of early interventions for high-risk populations in order to prioritize efforts to reduce cannabis use[1]. Instead, we should be inspired by the synergistic approaches implemented in other areas of medicine. Would we see a similar fight in cancer (i.e., scientists attacking each other's efforts in smoking cessation initiatives or screening programs versus surgical or medical treatment for cancer)? Our approach should be that it is important to intervene at all levels depicted above, and that we need studies, and preferably controlled trials, to identify the most effective interventions.

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Characterizing transdiagnostic premorbid biotypes can help progress in selective prevention in psychiatry

Fusar-Poli et al's insightful paper[1] is a timely appraisal of the foundations of preventive psychiatry. It is a call to action for our field to mount an individual, societal and global response to improve the lives of people with and those at risk for mental disorders. The authors outline a series of ambitious next steps in preventive psychiatry. They seek to advance this goal by integrating universal and targeted frameworks and by advancing our epidemiological knowledge of the multifactorial causation of mental disorders. An additional important step is to use such data toward developing stratified and personalized approaches. However, a major challenge in tackling these ambitious goals is the enormous heterogeneity of mental disorders, at symptomatic, pathophysiologic and etiologic levels. In this light, several strategies deserve consideration toward a successful move forward with Fusar-Poli et al's suggested next steps.

Any effort at prevention should first clarify what we are planning to prevent. For this reason, an accurate and valid diagnosis is critically important. As the authors point out, caseness is difficult to determine in psychiatry, because the disorders are defined based on symptoms, not on biology. For this reason, psychiatric diagnostic systems currently lack validity[2]. A biomarker-based nosology is clearly a critical next step toward stratification of populations meaningfully separating more homogeneous entities.

In a biomarker-driven effort to address the heterogeneity of psychotic disorders, investigators in the Bipolar-Schizophrenia Network on Intermediate Phenotypes (BSNIP) consortium recently used a K-means clustering approach to parse alterations in cognition and electrophysiology (event-related potentials and eye tracking) across the three major psychotic disorders: schizophrenia, schizoaffective disorder, and psychotic bipolar disorder.

Three distinct "biotypes" were identified which seemed orthogonal to the DSM-based categories[3]. Biotype 1 is characterized by severe cognitive impairments, reduced neural response to salient stimuli, marked gray matter reductions, social function deficits, more frequent family history of psychosis, and prominent negative symptoms. Biotype 2 is marked by moderate cognitive and social impairments and gray matter reductions, and by enhanced neural reactivity. Biotype 3 shows few neurobiological differences from healthy controls. These observations point to the possibility that biomarker-derived classifications may potentially better distinguish subtypes within the psychotic spectrum.

However, having a disease-related biomarker is not sufficient for early identification and prevention purposes, unless the biomarker is demonstrated to be present at illness onset or even before overt clinical manifestations of the disorders. This points to the potential value of identifying premorbid biotypes. Interestingly, biotype